

November 26, 1954

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Dear Ted:

Thank you for your provocative letter and note of the 18th. I hardly know why you would predict that I "won't like it". I had discussed the matter in very similar terms with both Paschkis and Klein but only by letter and I am looking forward to an opportunity of meeting them personally. George Klein's experiment seems very well to show that whatever is carried over in the chromatin transfer experiments included not only the quality of tumor formation but also much or all of the antigenic specificity of the donor tumor. Until one could more directly demonstrate that intact cells were present in the chromatin preparations one cannot of course rely upon their participation. The methodology becomes very much like that involved in bacterial recombination experiments, and for this obvious reason I have thought it advisable to include as many distinct genetic markers as possible. That still will not settle the matter finally until one can be sure whether there are or are not intact cells present.

I have wondered about still another approach. If intact cells are the agent, they might be expected to be resistant to DNAase, while if chromatin fragments are involved, this enzyme should inactivate them. It has been rebutted that the tissue fluids already contain ample DNAase, but this is not a sufficient argument in view of the success of Griffith's original experiments with pneumococci.

I like the design of your crucial experiment E. Has anyone done the first control experiment that you indicate, so that one could predict whether this test would be feasible?

From the substance of my correspondence with Klein and your own remarks under section D2 and 3, I would conclude that my most useful function at the discussions would not be so much a concrete review or discussion of Klein's own paper but rather a general presentation of the recent achievements of microbial genetic work insofar as they seem to point to analogous experimental possibilities with ascites tumor cells. Experiments on genetic transduction in a variety of bacteria would lend very strong theoretical support to the possibilities envisaged in your paragraph D2. Whether that possibility has actually been realized also in a tumor cell is of course the question that remains to be settled. By analogy with genetic transduction elsewhere, I would have expected that the chromatin-induced tumors would at least occasionally, if not invariably, show antigenic equivalence with the recipient rather than the donor cells. Possibly Klein's experiments were simply not extensive enough to discover a second antigenic category.

Yours sincerely,

Joshua Lederberg
Professor of Genetics

JL:mg